

### REMARKS

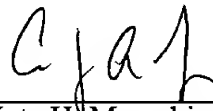
The claims have been amended to conform to applicants' election of group I. Claim 1 has been amended to insert the limitations of claims 10 and 13 and these claims have been cancelled as redundant. A species has been elected and claims 39 and 42 have been amended to depend from claim 1. Claim 42 has been limited as required to a single disclosed pathology of claim 44 and claims 43 and 44 are cancelled as redundant. No new matter has been added and prosecution on the merits is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Assistant Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to Deposit Account No. 03-1952 referencing docket No. 219002029000. However, the Assistant Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: June 18, 2001

By:

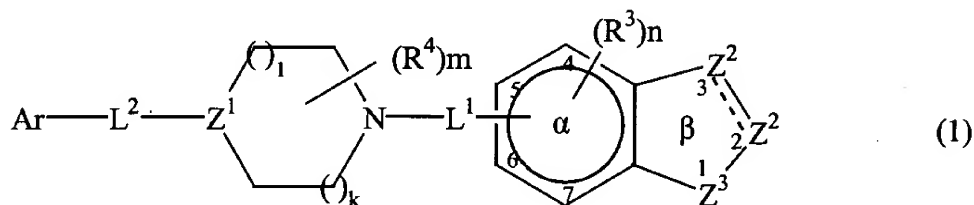


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# EXHIBIT A. - VERSION WITH MARKINGS TO SHOW CHANGES MADE

1. (Amended) A compound of the formula:



and the pharmaceutically acceptable salts thereof, or a pharmaceutical composition thereof, wherein

 represents a single or double bond;

one  $Z^2$  is CA or  $CR^8A$  and the other is  $CR^1$ ,  $CR^1_2$ ,  $NR^6$  or N wherein each  $R^1$ ,  $R^6$  and  $R^8$  is independently hydrogen or noninterfering substituent;

A is  $-W_i-COXY$  wherein Y is  $COR^2$  or an isostere thereof and  $R^2$  is hydrogen or a noninterfering substituent, each of W and X is a spacer of 2-6Å, and each of i and j is independently 0 or 1;

$Z^3$  is  $NR^7$  or O;

each  $R^3$  is independently a noninterfering substituent;

n is 0-3;

each of  $L^1$  and  $L^2$  is a linker;

each  $R^4$  is independently a noninterfering substituent;

m is 0-4;

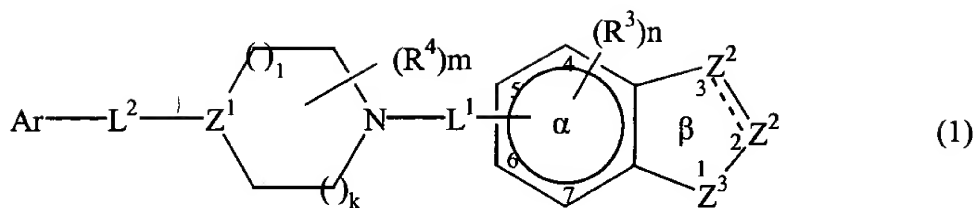
$Z^1$  is  $[CR^5 \text{ or } N]$  [wherein  $R^5$  is hydrogen or a noninterfering substituent];

each of l and k is [an integer from 0-2 wherein the sum of l and k is 0-3] 1;

Ar is an aryl group substituted with 0-5 noninterfering substituents, wherein two noninterfering substituents can form a fused ring; and

the distance between the atom of Ar linked to  $L^2$  and the center of the  $\alpha$  ring is 4.5-24Å.

39. (Amended) A pharmaceutical composition for treating conditions characterized by enhanced p38- $\alpha$  activity which composition comprises  
a therapeutically effective amount of a compound claim 1 or [of the formula



and] the pharmaceutically acceptable salts thereof, along with a pharmaceutically acceptable excipient [or a pharmaceutical composition thereof, wherein

 represents a single or double bond;

one  $Z^2$  is CA or  $CR^8A$  and the other is  $CR^1$ ,  $CR^1_2$ ,  $NR^6$  or N wherein each  $R^1$ ,  $R^6$  and  $R^8$  is independently hydrogen or noninterfering substituent;

A is  $-W_i-CO_jY$  wherein Y is  $COR^2$  or an isostere thereof and  $R^2$  is hydrogen or a noninterfering substituent, each of W and X is a spacer of 2-6Å, and each of i and j is independently 0 or 1;

$Z^3$  is  $NR^7$  or O;

each  $R^3$  is independently a noninterfering substituent;

n is 0-3;

each of  $L^1$  and  $L^2$  is a linker;

each  $R^4$  is independently a noninterfering substituent;

m is 0-4;

$Z^1$  is  $CR^5$  or N wherein  $R^5$  is hydrogen or a noninterfering substituent;

each of l and k is an integer from 0-2 wherein the sum of l and k is 0-3;

Ar is an aryl group substituted with 0-5 noninterfering substituents, wherein two noninterfering substituents can form a fused ring; and

the distance between the atom of Ar linked to  $L^2$  and the center of the  $\alpha$  ring is 4.5-24Å].

42. (Amended) A method to treat rheumatoid arthritis [a condition mediated by p38- $\alpha$  kinase] comprising administering to a subject in need of such treatment a compound of claim 1 or [the formula:



 represents a single or double bond;

A is  $-W_i-CO-X_jY$  wherein Y is  $COR^2$  or an isostere thereof and  $R^2$  is hydrogen or a interfering substituent, each of W and X is a spacer of 2-6Å, and each of i and j is independently 0 or 1;

each R<sup>3</sup> is independently a noninterfering substituent;

each of  $L^1$  and  $L^2$  is a linker;

each R<sup>4</sup> is independently a noninterfering substituent;

m is 0-4;

**Z<sup>1</sup> is CR<sup>5</sup> or N wherein R<sup>5</sup> is hydrogen or a noninterfering substituent;**

each of l and k is an integer from 0-2 wherein the sum of l and k is 0-3;

Ar is an aryl group substituted with 0-5 noninterfering substituents, wherein two noninterfering substituents can form a fused ring; and

the distance between the atom of Ar linked to L<sup>2</sup> and the center of the  $\alpha$  ring is 4.5-24Å].